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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

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Supplementary Appendix

Contents

1. Supplementary Method

1.1 Enzyme-linked immunosorbent assay (ELISA) for anti-SARS-CoV-2 IgG

The detection was performed by National Institutes for Food and Drug Control using ELISA kits (Wantai BioPharm, Beijing, China).
Add serum samples to be tested and negative and positive control samples to the microplates coated with SARS-CoV-2 antigen, set blank control wells for each plate, incubate and wash, then add enzyme-labeled reagent containing HRP-labeled anti-human IgG antibody, incubate and wash again, then add chromogen solutions A and B to each well, incubate, and then add stop solution. Set the wavelength of microplate reader at 450 nm (it is recommended to use double wavelength of 450 nm / 600-650 nm for detection. If the detection is conducted using double wavelength, blank control wells may not be set), and adjust to zero point with the blank well, then measure the A value of each well. On the premise that negative and positive controls are established, cut-off value is calculated, and whether there is anti-SARS-CoV-2 IgG antibody in the specimen is assessed according to the Cutoff value. The maximum dilution assessed as positive is the antibody titer of the sample. The cut-off value of positive titer is 2, and a two-fold increase in titer post-vaccination from baseline is considered to be seroconversion.

1.2 Enzyme-linked immunosorbent assay (ELISA) for anti-SARS-CoV-2 secretory IgA

The detection was performed by National Institutes for Food and Drug Control using ELISA kits (Wantai BioPharm, Beijing, China).
Add nasopharyngeal swabs to be tested and negative and positive control specimens to the microplates coated with SARS-CoV-2 antigen, set blank control wells for each plate, incubate and wash, then add enzyme-labeled reagent containing HRP-labeled anti-human IgA antibody, incubate and wash again, then add chromogen solutions A and B to each well, incubate, and then add stop solution. Set the wavelength of microplate reader at 450 nm (it is recommended to use double wavelength of 450 nm / 600 - 650 nm for detection. If the detection is conducted using double wavelength, blank control wells may not be set), and adjust to zero point with the blank well, then measure the A value of each well. On the premise that negative and positive controls are established, Cutoff value is calculated, and whether there is anti-SARS-CoV-2 antibody in the specimen is assessed according to the cut-off value. The maximum dilution assessed as positive is the antibody titer of the sample. The cut-off value of positive titer is 2, and a two-fold increase in titer post-vaccination from baseline is considered to be positive conversion.

1.3 Enzyme-linked immunosorbent assay (ELISA) for anti-H1N1 IgG

The detection was performed by National Institutes for Food and Drug Control.
Add serum samples to be tested and negative and positive control specimens to the microplates coated with influenza virus antigen, set blank control wells for each plate, incubate and wash, then add enzyme-labeled reagent containing HRP-labeled anti-human IgG antibody, incubate

and wash again, then add chromogen solutions A and B to each well, incubate, and then add stop solution. Set the wavelength of microplate reader at 450 nm (it is recommended to use double wavelength of 450 nm / 600 - 650 nm for detection. If the detection is conducted using double wavelength, blank control wells may not be set), and adjust to zero point with the blank well, then measure the A value of each well. On the premise that negative and positive controls are established, Cutoff value is calculated, and whether there is anti-H1N1 IgG antibody in the specimen is assessed according to the cut-off value. The maximum dilution assessed as positive is the antibody titer of the sample. The cut-off value of positive titer is 2, and a two-fold increase in titer post-vaccination from baseline is considered to be seroconversion.

1.4 Enzyme-linked immunosorbent assay (ELISA) for anti-H1N1 secretory IgA

The detection was performed by National Institutes for Food and Drug Control.
Add nasopharyngeal swabs to be tested and negative and positive control specimens to the microplates coated with influenza virus antigen, set blank control wells for each plate, incubate and wash, then add enzyme-labeled reagent containing HRP-labeled anti-human IgA antibody, incubate and wash again, then add chromogen solutions A and B to each well, incubate, and then add stop solution. Set the wavelength of microplate reader at 450 nm (it is recommended to use double wavelength of 450 nm / 600 - 650 nm for detection. If the detection is conducted using double wavelength, blank control wells may not be set), and adjust to zero point with the blank well, then measure the A value of each well. On the premise that negative and positive controls are established, Cutoff value is calculated, and whether there is anti-influenza virus IgA antibody in the specimen is assessed according to the Cutoff value. The maximum dilution assessed as positive is the antibody titer of the sample. The cut-off value of positive titer is 2, and a two-fold increase in titer post-vaccination from baseline is considered to be positive conversion.

1.5 IFN-γ enzyme-linked immunospot (ELISpot) assay

The detection was performed by Jiangsu Huatai Vaccine Engineering Technology Research Co. LTD. on fresh peripheral blood mononuclear cells (PBMCs), using a human IFN-γ ELISpot Kit following the manufacturer's instructions.
By stimulating and culturing PBMCs, the number of spots formed by IFN-γ secreted by cells in ELISpot microplate is detected, thus indicating the response of T cells. 200μL of serum-free medium is added to each well, which is placed at room temperature for 10 min to activate the pre-coated plate. After that, the medium is discarded. The isolated PBMCs are adjusted to the required concentration, and added to each test well at 100μL/well. Among them, 100,000 cells are added to positive control wells with 25 ng of PHA-M; 500,000 cells are added to negative control wells; background negative controls are added with serum-free media containing 0.05% DMSO; the test wells are added with 500,000 cells and 10μL of SARS-CoV-2 spike peptide pool. After that, the plate is covered and wrapped by aluminum foil paper, and then placed into a 37℃ 5% CO_2 incubator for 22 ± 2h. After the culture, the cell suspension in the wells is discarded, and each well is washed 6 times, standing 1 min for every wash, and then inverted and dried on absorbent paper. Detection antibody is added to each well and incubated for 1 h. After the plate is repeatedly washed for 6 times, Streptavidin-HRP is added to each well and

incubated for 1 h. After plate washing is repeated for 6 times, 100μL of substrate solution is added to each well for reaction at room temperature for 30 min in darkness. Finally, the color development is stopped with deionized water, and the plate is placed in a cool place and dried in the air. The numbers of spots on ELISPOT plates were calculated and read by AID EliSpot Reader (AID IspotELR071). IFN-γ secreting cells per 10^6 PBMCs at each data point represents the mean number of spots from stimulated wells for one participant, after subtraction of the unstimulated control, and values less than 1 are corrected to 1.

1.6 Viral shedding detection

The detection is performed by National Institutes for Food and Drug Control using RT-PCR technique.

The nucleic acids in samples are extracted by nucleic acid extraction kit. Specific primer probes are designed for the virus strain of influenza virus vector (NEP) to quantitatively detect the vaccine strain RNA in nasopharyngeal swabs and serum by RT-PCR. At the same time, the method could effectively prevent false-negative results by setting internal standard (processed in parallel with the specimens) and monitoring the whole process of the test. The NEP RT-PCR (+) samples were cultured, and NEP gene was tested again after cell passage. If the samples were still tested positive, RBD gene and NS1 gene were tested for final identification of virus strains.

1.7 Environmental sampling and detection

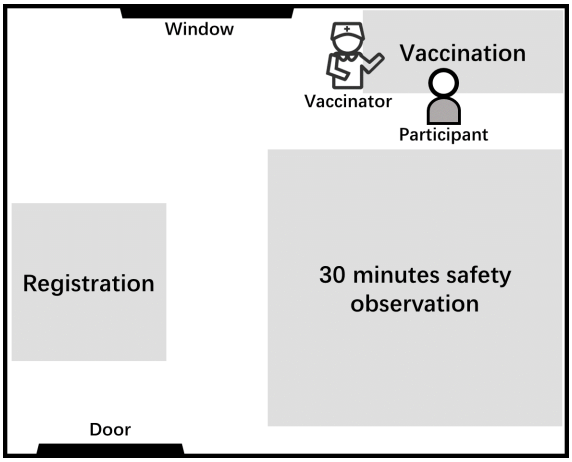
The environmental Institute of Jiangsu CDC was responsible for the on-site sampling work, and Institute of Pathogenic Microbiology, Jiangsu CDC was responsible for sample detection. In order to maintain the blind state, the room number corresponding to the detection result is re-coded by the tester.

Air samples:

Air samples were collected using the professional equipment (ASE-200p, Shenzhen Longsi Medical Technology Co., Ltd., Shenzhen, China) at a total of 10 time points, including before, during and after vaccination in four vaccination rooms. Sampling sites of air were mainly distributed near the seat of the participant (including the vaccination area and safety observation area), and the sampling height was near the nose of the participant. Each sample took 10 minutes with a flow rate of 200L/min. And three tubes (about 9ml) of double antibody-contained collection solution (YM-B, Jiangsu Yimi Biological Technology Co., Ltd.) were used for each air sample. After the collection, the samples were transferred to the virus sampling tube with a sterile pipetting gun for preservation.

Object surface samples:

Samples were collected from the outer surface of the vaccinator's latex gloves (back of hand), the masks of the vaccinators, the masks of the participants, the working tables and the ground of the working areas, respectively, by using a viable virus sampling tube containing double antibodies (YM-B, Jiangsu Yimi Biological Technology Co., Ltd.).



Vaccination room layout

2. Supplementary Figure

Figure S1. Incidence of adverse reactions following vaccination.

Adverse reactions refer to the adverse events related to the vaccination reported within 30 (phase 1) or 42 days (phase 2 and ECT). The severity of adverse events was graded as grade 1, grade 2, grade 3, or grade 4 according to the scale issued by the China National Medical Products of Administration and U.S. Department of Health and Human Service. In these trials, only four cases of grade 3 adverse reactions (three fever and one diarrhea) in the vaccine groups and no cases of grade 4 were reported. Some uncommon symptoms including local and systemic are not shown in the figure but listed in Table S1-S3.

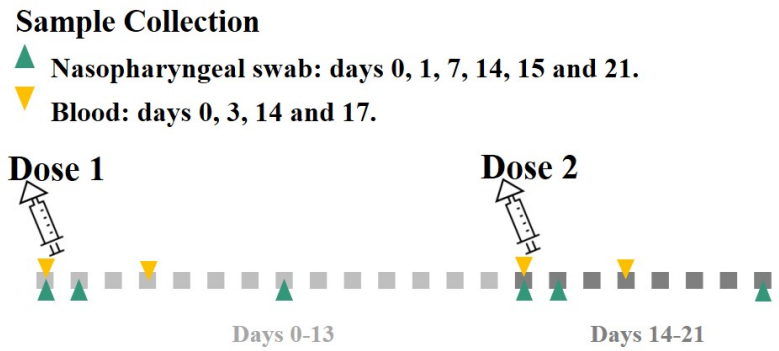


Figure S2. Evaluation for viral shedding of the vaccine strain.

The dotted line indicates days post the 1st-dose vaccination. And the light gray and dark gray parts of the line indicate the observation period of viral shedding after the initial dose and booster (at day 14), respectively.

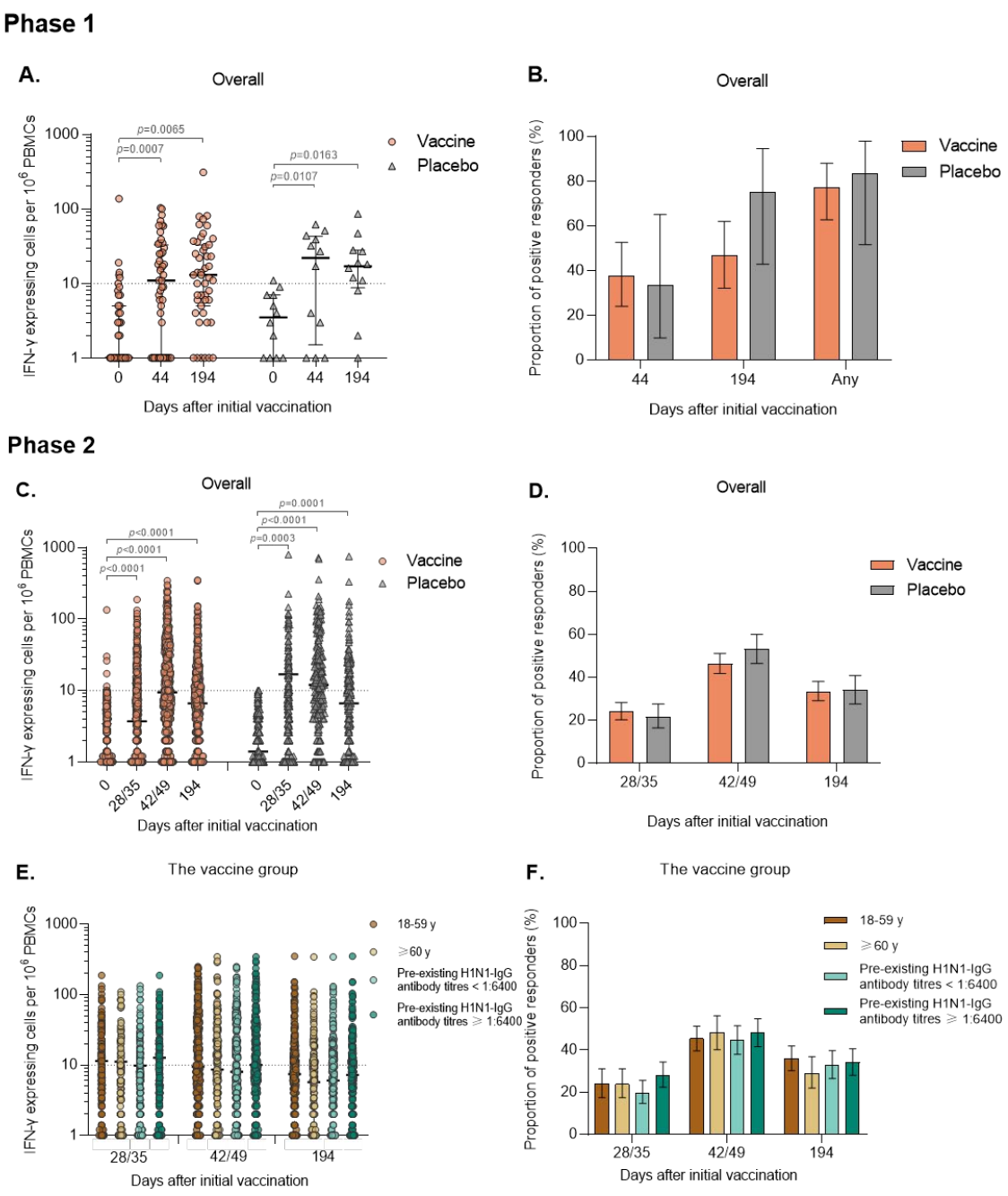


Figure S3. SARS-CoV-2 spike protein-specific cellular immune response following vaccination in phases 1 and 2.

IFN-γ secreting cells per 10^6 PBMCs at each data point represents the mean number of spots from duplicate (phase 1) or triplicate (phase 2) stimulated wells for one participant, after subtraction of the unstimulated control, and values less than 1 were corrected to 1. The results were considered positive if the number of spots in stimulated well increased at least 2·1 times as much as that in unstimulated control and the IFN-γ secreting cells per 10^6 PBMCs >10 (indicated with the dotted line in the figure). Error bars show the interquartile range. The p value was analyzed by paired t test. IFN-γ: Interferon gamma. ELISpot: enzyme-linked immunospot. PBMCs: peripheral blood mononuclear cell.

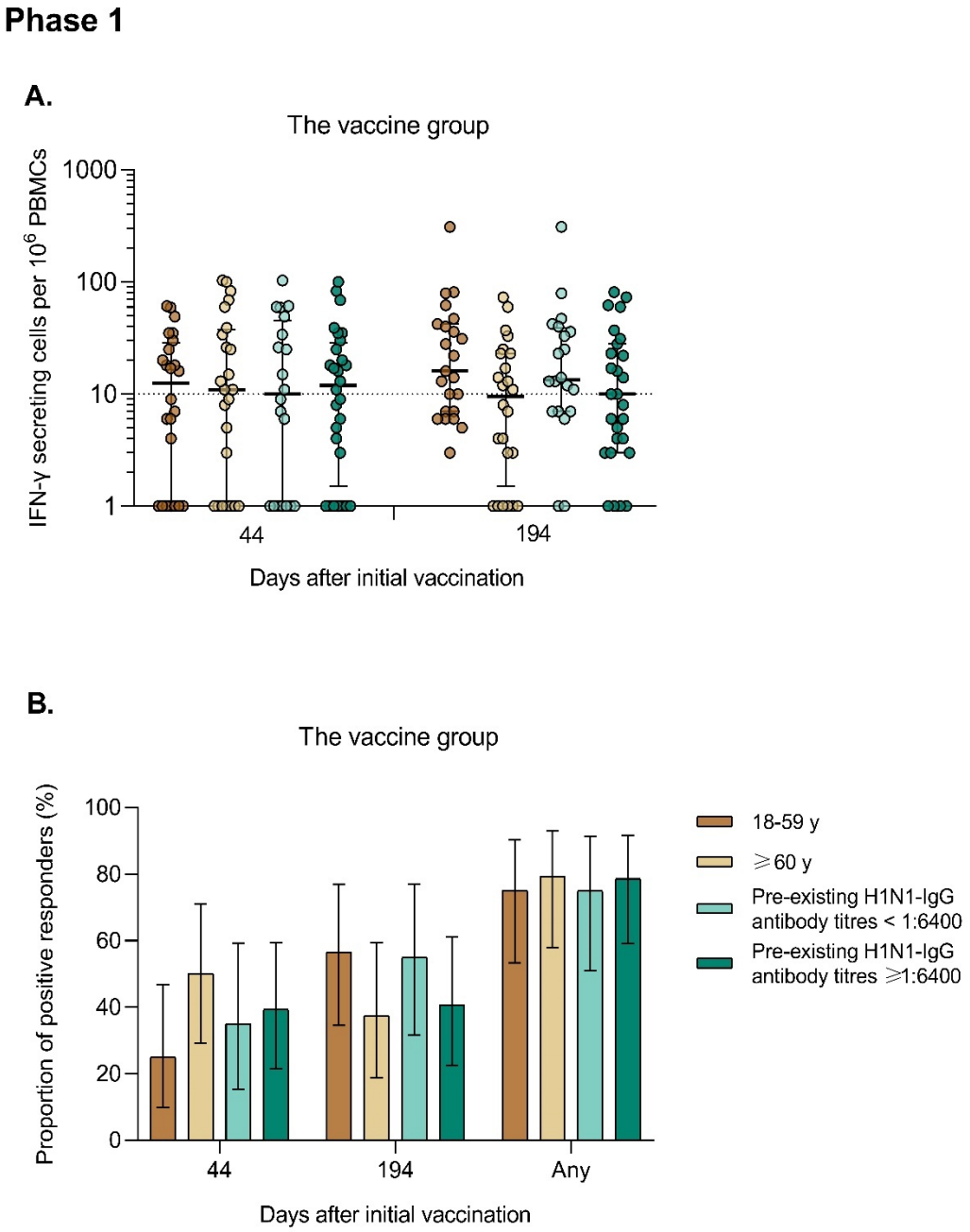


Figure S4. SARS-CoV-2 spike protein-specific cellular immune response following vaccination in phase 1 (stratification analysis by age and pre-existing H1N1-IgG antibody).

IFN-γ secreting cells per 10^6 PBMCs at each data point represents the mean number of spots from duplicate stimulated wells for one participant, after subtraction of the unstimulated control, and values less than 1 were corrected to 1. The results were considered positive if the number of spots in stimulated well increased at least 2·1 times as much as that in unstimulated control and the IFN-γ secreting cells per 10^6 PBMCs >10 (indicated with the dotted line in the figure). Error bars show the interquartile range. IFN-γ: Interferon gamma. ELISpot: enzyme-linked immunospot. PBMCs: peripheral blood mononuclear cell.

Phase 2

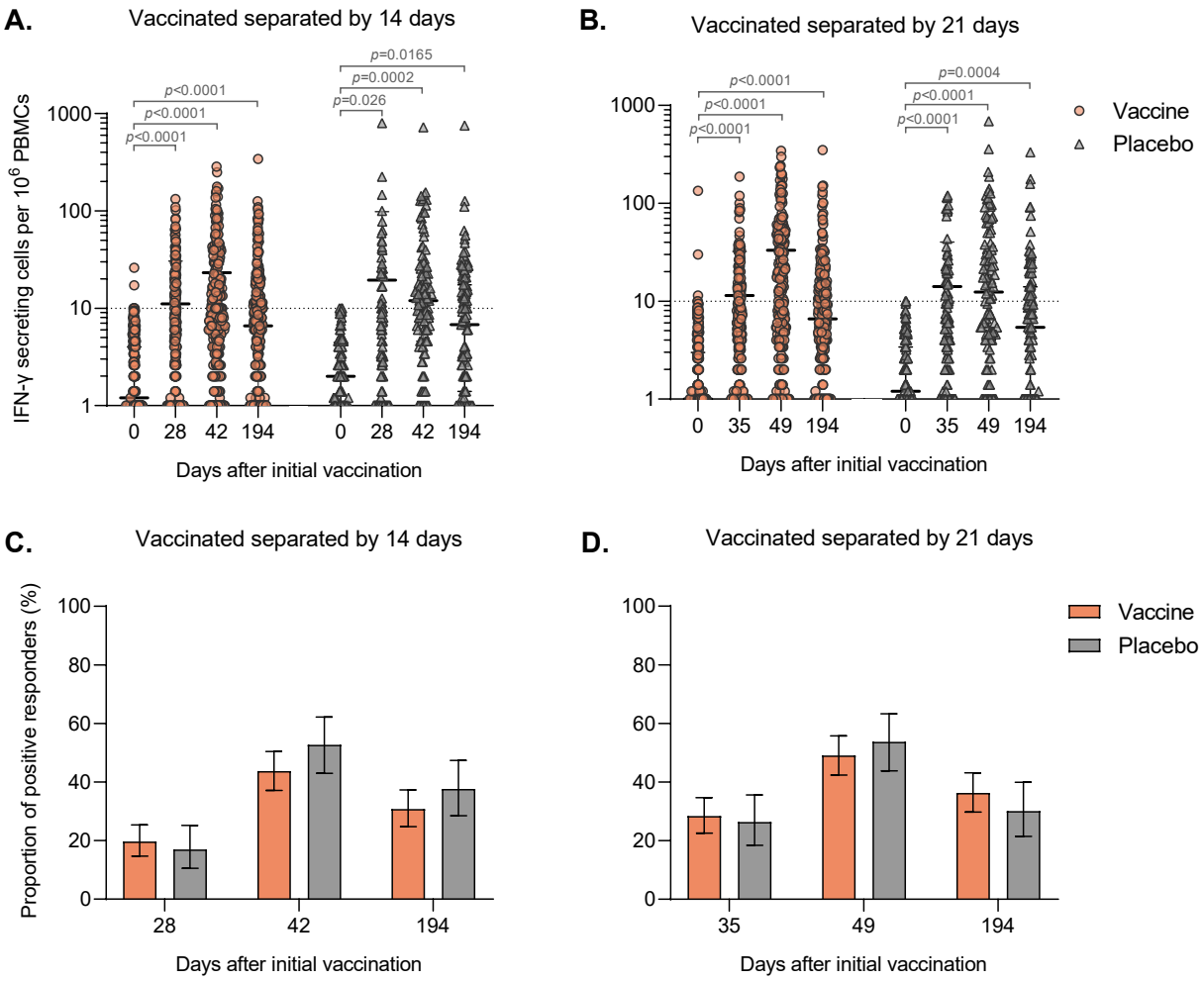


Figure S5. SARS-CoV-2 spike protein-specific cellular immune response following vaccination in phase 2 (stratification analysis by vaccination schedule)

Legend:

IFN-γ secreting cells per 10^6 PBMCs at each data point represents the mean number of spots from triplicate stimulated wells for one participant, after subtraction of the unstimulated control, and values less than 1 were corrected to 1. The results were considered positive if the number of spots in stimulated well increased at least 2·1 times as much as that in unstimulated control and the IFN-γ secreting cells per 10^6 PBMCs >10 (indicated with the dotted line in the figure). Error bars show the interquartile range. The *p* value was analyzed by paired t test. IFN-γ: Interferon gamma. ELISpot: enzyme-linked immunospot. PBMCs: peripheral blood mononuclear cell.

3. Supplementary Tables

Table S1. Adverse events following vaccination in phase 1.

	The vaccine group (N=51) n (%)			The placebo group (N=12) n (%)		
	Any	Grade 1	Grade 2	Any	Grade 1	Grade 2
All adverse reactions within 30 days after vaccination						
	10 (20%)	7 (14%)	3 (6%)	2 (17%)	2 (17%)	0
Any local reactions	3 (6%)	2 (4%)	1 (2%)	1 (8%)	1 (8%)	0
Itchy nose	1 (2%)	1 (2%)	0	0	0	0
Pharyngalgia	0	0	0	1 (8%)	1 (8%)	0
Sneeze	1 (2%)	0	1 (2%)	0	0	0
Oropharyngeal discomfort	1 (2%)	1 (2%)	0	0	0	0
Any systemic reactions	7 (14%)	4 (8%)	3 (6%)	2 (17%)	2 (17%)	0
Fever	1 (2%)	1 (2%)	0	0	0	0
Headache	4 (8%)	2 (4%)	2 (4%)	0	0	0
Cough	0	0	0	1 (8%)	1 (8%)	0
Fatigue	3 (6%)	3 (6%)	0	0	0	0
Myalgia	1 (2%)	1 (2%)	0	0	0	0
Abdominal pain	1 (2%)	0	1 (2%)	2 (17%)	2 (17%)	0
Arthralgia	1 (2%)	0	1 (2%)	0	0	0
Upper respiratory infection	1 (2%)	0	1 (2%)	0	0	0
All adverse events within 30 days after vaccination						
	11 (22%)	8 (16%)	3 (6%)	4 (33%)	2 (17%)	2 (17%)

N: the number of participants vaccinated any dose. n: the number of participants reporting adverse event.

Table S2. Adverse events following vaccination in phase 2.

	The vaccine group (N=485) n (%)				The placebo group (N=239) n (%)			
	Any	Grade 1	Grade 2	Grade 3	Any	Grade 1	Grade 2	Grade 3
All adverse reactions within 42 days after vaccination								
	102 (21%)	87 (18%)	11 (2%)	4 (1%)	56 (23%)	48 (20%)	8 (3%)	0
Any local reactions	44 (9%)	39 (8%)	5 (1%)	0	26 (11%)	24 (10%)	2 (1%)	0
Rhinorrhea	30 (6%)	27 (6%)	3 (1%)	0	22 (9%)	20 (8%)	2 (1%)	0
Nasal congestion	9 (2%)	8 (2%)	1 (0%)	0	13 (5%)	12 (5%)	1 (0%)	0
Itchy nose	8 (2%)	8 (2%)	0	0	2 (1%)	2 (1%)	0	0
Pharyngalgia	8 (2%)	5 (1%)	3 (1%)	0	5 (2%)	5 (2%)	0	0
Sneeze	2 (0%)	2 (0%)	0	0	1 (0%)	1 (0%)	0	0
Epistaxis	1 (0%)	1 (0%)	0	0	2 (1%)	2 (1%)	0	0
Rhinalgia	0	0	0	0	1 (0%)	1 (0%)	0	0
Oropharyngeal discomfort	0	0	0	0	1 (0%)	1 (0%)	0	0
Any systemic reactions	78 (16%)	64 (13%)	10 (2%)	4 (1%)	42 (18%)	34 (14%)	8 (3%)	0
Fever	33 (7%)	30 (6%)	0	3 (1%)	19 (8%)	18 (8%)	1 (0%)	0
Fatigue	16 (3%)	15 (3%)	1 (0%)	0	12 (5%)	10 (4%)	2 (1%)	0
Headache	12 (2%)	11 (2%)	1 (0%)	0	12 (5%)	12 (5%)	0	0
Dizzy	10 (2%)	10 (2%)	0	0	6 (3%)	5 (2%)	1 (0%)	0
Cough	18 (4%)	14 (3%)	4 (1%)	0	11 (5%)	8 (3%)	3 (1%)	0
Nausea	7 (1%)	6 (1%)	1 (0%)	0	4 (2%)	4 (2%)	0	0
Diarrhea	5 (1%)	2 (0%)	2 (0%)	1 (0%)	2 (1%)	1 (0%)	1 (0%)	0
Vomiting	5 (1%)	3 (1%)	2 (0%)	0	0	0	0	0
Abdominal pain	2 (0%)	0	2 (0%)	0	0	0	0	0
Myalgia	6 (1%)	4 (1%)	2 (0%)	0	4 (2%)	3 (1%)	1 (0%)	0
Leg aches	0	0	0	0	1 (0%)	1 (0%)	0	0
Anorexia	1 (0%)	1 (0%)	0	0	0	0	0	0

Allergic reaction	1 (0%)	0	1 (0%)	0	0	0	0	0
Pruritus	1 (0%)	0	1 (0%)	0	0	0	0	0
Chest discomfort	1 (0%)	1 (0%)	0	0	0	0	0	0
Palpitation	1 (0%)	1 (0%)	0	0	0	0	0	0
All adverse events within 42 days after vaccination								
	130 (27%)	88 (18%)	34 (7%)	8 (2%)	71 (30%)	49 (21%)	22 (9%)	0

N: the number of participants vaccinated any dose. n: the number of participants reporting adverse event.

Table S3. Adverse events following vaccination in phase 2 extension clinical trial (subgroup).

	The vaccine group (N=148) n (%)				The placebo group (N=149) n (%)			
	Any	Grade 1	Grade 2	Grade 3	Any	Grade 1	Grade 2	Grade 3
All adverse reactions within 42 days after vaccination								
	21 (14%)	18 (12%)	3 (2%)	0	28 (19%)	25 (17%)	2 (1%)	1 (1%)
Any local reactions	8 (5%)	7 (5%)	1 (1%)	0	10 (7%)	8 (5%)	2 (1%)	0
Rhinorrhea	4 (3%)	3 (2%)	1 (1%)	0	5 (3%)	5 (3%)	0	0
Itchy nose	4 (3%)	4 (3%)	0	0	4 (3%)	4 (3%)	0	0
Nasal congestion	1 (1%)	1 (1%)	0	0	2 (1%)	2 (1%)	0	0
Pharyngalgia	0	0	0	0	3 (2%)	1 (1%)	2 (1%)	0
Rhinalgia	0	0	0	0	2 (1%)	2 (1%)	0	0
Any systemic reactions	18 (12%)	16 (11%)	2 (1%)	0	25 (17%)	23 (15%)	1 (1%)	1 (1%)
Fever	8 (5%)	7 (5%)	1 (1%)	0	11 (7%)	10 (7%)	0	1 (1%)
Fatigue	1 (1%)	1 (1%)	0	0	5 (3%)	5 (3%)	0	0
Headache	3 (2%)	3 (2%)	0	0	8 (5%)	7 (5%)	1 (1%)	0
Dizzy	1 (1%)	1 (1%)	0	0	2 (1%)	2 (1%)	0	0
Cough	1 (1%)	1 (1%)	0	0	3 (2%)	2 (1%)	1 (1%)	0
Nausea	0	0	0	0	1 (1%)	0	1 (1%)	0
Diarrhea	3 (2%)	3 (2%)	0	0	3 (2%)	3 (2%)	0	0
Vomiting	0	0	0	0	1 (1%)	1 (1%)	0	0
Myalgia	0	0	0	0	6 (4%)	6 (4%)	0	0
Blurred vision	1 (1%)	1 (1%)	0	0	0	0	0	0
Allergic reaction	2 (1%)	1 (1%)	1 (1%)	0	2 (1%)	2 (1%)	0	0
All adverse events within 42 days after vaccination								
	25 (17%)	17 (11%)	7 (5%)	1 (1%)	34 (23%)	22 (15%)	10 (7%)	2 (1%)

N: the number of participants vaccinated any dose. n: the number of participants reporting adverse event.

Table S4. List of serious adverse events throughout the study period.

Trial	Subject ID	Serious Adverse Event	Group	Vaccine correlation
phase 1	1135	Malignant tumor of brain	Vaccine	Unrelated
phase 2	10196	third-degree burn	Vaccine	Unrelated
	10237	Incised injury of left thumb	Vaccine	Unrelated
	10271	Acute purulent appendicitis	Vaccine	Unrelated
		Bronchiectasis with infection		Unrelated
	10572	Synovial plica syndrome of left knee	Placebo	Unrelated
		Traumatic double knee arthropathy		Unrelated
	10638	Cerebral infarction	Vaccine	Unrelated
		Left facial neuritis		Unrelated
	10317	Acute exacerbation of chronic obstructive pulmonary disease	Vaccine	Unrelated
	10675	Left ureteral calculi	Vaccine	Unrelated
	10409	Hemangioma of nasal septum	Vaccine	Unrelated
	10114	Hepatic hemangioma	Vaccine	Unrelated
	10339	Acute calculous cholecystitis	Vaccine	Unrelated
	10521	Papillary carcinoma of left thyroid	Vaccine	Unrelated
	10382	Left femoral intertrochanteric fracture	Vaccine	Unrelated
	10322	Cecal carcinoma T4N2M1 IVB stage (lung, liver)	Vaccine	Unrelated
	10145	Duodenal ulcer bleeding	Placebo	Unrelated
	10494	Left ankle fracture	Placebo	Unrelated
	10157	Right femoral neck fracture	Vaccine	Unrelated
	10164	Right hip osteoarthritis	Placebo	Unrelated
	10238	Lumbosacral spinal stenosis	Placebo	Unrelated
	10277	Left breast invasive breast cancer (p-T1cN1aM0 IIA stage)	Vaccine	Unrelated
	10337	Right occipital herpes zoster	Placebo	Unrelated

	10480	Sciatic fracture	Vaccine	Unrelated
Extension clinical trial*	1283	Left femoral neck fracture	Unknown	Unrelated
	1374	Gallstone	Unknown	Unrelated
		Gangrenous cholecystitis	Unknown	Unrelated
	1123	Cerebral infarction	Unknown	Unrelated

*Extension clinical trial is ongoing and have not yet been unblinded.

Table S5. Laboratory Abnormalities on Day 3 after vaccination.

Dose	Laboratory measures	Severity	The vaccine group (N=51) n (%)	The placebo group (N=12) n (%)
Total	Any Laboratory index		2 (4%)	0
		Grade 1	2 (4%)	0
		Grade 2 or above	0	0
	Urine protein		1 (2%)	0
	Blood glucose		1 (2%)	0
Dose 1	Any Laboratory index		1 (2%)	0
	Blood glucose		1 (2%)	0
Dose 2	Any Laboratory index		1 (2%)	0
	Urine protein		1 (2%)	0

N: the number of participants vaccinated any dose. n: the number of participants reporting laboratory abnormality.

Table S6. The proportion of specific T-cell immune responders in PBMCs in phase 1 (PPS-I).

Time after the second dose	Participants	Vaccine			Placebo			*P* value†
		Responder* %(n/N)	95%CI	*P* value†	Responder* %(n/N)	95%CI	*P* value†	
30 days								
	Total	38% (18/48)	24·0%, 52·6%	-	33% (4/12)	9·9%, 65·1%	-	>0·99
	18-59 y	25% (6/24)	9·8%, 46·7%	0·07	17% (1/6)	0·4%, 64·1%	0·55	>0·99
	≥ 60 y	50% (12/24)	29·1%, 70·9%		50% (3/6)	11·8%, 88·2%		>0·99
	Pre-existing H1N1-IgG antibody titres < 1:6400	35% (7/20)	15·4%, 59·2%	0·76	43% (3/7)	9·9%, 81·6%	0·58	>0·99
	Pre-existing H1N1-IgG antibody titres ≥ 1:6400	39% (11/28)	21·5%, 59·4%		20% (1/5)	0·5%, 71·6%		0·63
6 months								
	Total	47% (22/47)	32·1%, 61·9%	-	75% (9/12)	42·8%, 94·5%	-	0·08
	18-59 y	57% (13/23)	34·5%,76·8%	0·19	83% (5/6)	35·9%, 99·6%	>0.99	0·36
	≥ 60 y	38% (9/24)	18·8%, 59·4%		67% (4/6)	22·3%, 95·7%		0·36
	Pre-existing H1N1-IgG antibody titres < 1:6400	55% (11/20)	31·5%, 76·9%	0·33	86% (6/7)	42·1%, 99·6%	0·52	0·20
	Pre-existing H1N1-IgG antibody titres ≥ 1:6400	41% (11/27)	22·4%, 61·2%		60% (3/5)	14·7%, 94·7%		0·63

PBMCs: peripheral blood mononuclear cells. PPS-I: the per-protocol set for immunogenicity; except for three participants with cross-reactivity at baseline, 60 participants were included in the PPS-I of cellular immunity. N: the number of participants in PPS-I. n: the number of responders. CI: confidence interval. *Responders: negative at baseline and positive after vaccination.

† χ^2 test or Fisher's exact test was used to compare the response rates of cellular immunity after vaccination between the groups.

Table S7. The level of spot-forming cells per million PBMCs for IFN-γ in PBMCs of responders* in phase 1 (PPS-I).

Time after the second dose	Participants	Vaccine		Placebo		*P* value†
		n	Median (IQR)	n	Median (IQR)	
30 days						
	Total	18	32·0 (18·0, 61·0)	4	29·5 (22·0, 35·5)	0·73
	18-59 y	6	25·0 (18·0, 35·0)	1	39·0 (39·0, 39·0)	0·45
	≥ 60 y	12	36·5 (20·0, 76·0)	3	27·0 (17·0, 32·0)	0·28
	Pre-existing H1N1-IgG antibody titres < 1:6400	7	34·0 (25·0, 64·0)	3	27·0 (17·0, 32·0)	0·29
	Pre-existing H1N1-IgG antibody titres ≥ 1:6400	11	30·0 (18·0, 69·0)	1	39·0 (39·0, 39·0)	0·66
6 months						
	Total	22	29·5 (17·0, 60·0)	9	19·0 (16·0, 28·0)	0·29
	18-59 y	13	40·0 (23·0, 62·0)	5	27·0 (18·0, 28·0)	0·55
	≥ 60 y	9	23·0 (17·0, 33·0)	4	15·5 (11·5, 33·0)	0·28
	Pre-existing H1N1-IgG antibody titres < 1:6400	11	33·0 (14·0, 47·0)	6	27·5 (12·0, 47·0)	0·54
	Pre-existing H1N1-IgG antibody titres ≥ 1:6400	11	28·0 (17·0, 62·0)	3	18·0 (16·0, 19·0)	0·19

PBMCs: peripheral blood mononuclear cells. PPS-I: the per-protocol set for immunogenicity. n: the number of responders. IQR: interquartile range.

† Wilcoxon rank sum test was used to compare the level of cellular immunity after vaccination between the groups.

*Responders: negative at baseline and positive after vaccination.

Table S8. The proportion of specific T-cell immune responders[*] in PBMCs in phase 2 (PPS-I).

Time after the second dose	Participants	Vaccine			Placebo			*P* value[†]
		Responder[*] %(n/N)	95%CI	*P* value[†]	Responder[*] %(n/N)	95%CI	*P* value[†]	
14 days								
	Total	24% (110/458)	20·2%，28·2%	-	22% (48/222)	16·4%，27·6%	-	0·49
	18-59 y	24% (72/298)	19·4%，29·4%	0·92	20% (29/146)	13·7%，27·3%	0·38	0·31
	≥ 60 y	24% (38/160)	17·4%，31·1%		25% (19/76)	15·8%，36·3%		0·83
	Pre-existing H1N1-IgG antibody titres < 1:6400	20% (44/223)	14·7%，25·6%	0·04	17% (19/111)	10·6%，25·4%	0·10	0·57
	Pre-existing H1N1-IgG antibody titres ≥ 1:6400	28% (66/235)	22·4%，34·3%		26% (29/111)	18·3%，35·3%		0·70
28 days								
	Total	46% (211/455)	41·7%，51·1%	-	53% (117/220)	46·4%，59·9%	-	0·097
	18-59 y	45% (134/295)	39·6%，51·3%	0·58	53% (77/144)	45·0%，61·8%	0·91	0·11
	≥ 60 y	48% (77/160)	40·2%，56·2%		53% (40/76)	40·8%，64·2%		0·52
	Pre-existing H1N1-IgG antibody titres < 1:6400	45% (99/222)	37·9%，51·4%	0·46	58% (63/109)	48·0%，67·2%	0·17	0·024
	Pre-existing H1N1-IgG antibody titres ≥ 1:6400	48% (112/233)	41·5%，54·7%		49% (54/111)	39·1%，58·3%		0·92
6 months								
	Total	33% (146/436)	29·1%，38·1%	-	34% (72/212)	27·6%，40·8%	-	0·90
	18-59 y	36% (101/281)	30·3%，41·9%	0·14	35% (47/135)	26·8%，43·5%	0·73	0·82
	≥ 60 y	29% (45/155)	22·0%，36·9%		33% (25/77)	22·2%，44·1%		0·59

Pre-existing H1N1-IgG antibody titres < 1:6400	33% (68/207)	26·5%，39·7%	0·79		34% (36/105)	25·3%，44·2%	0·92	0·80
Pre-existing H1N1-IgG antibody titres ≥ 1:6400	34% (78/229)	28·0%，40·6%			34% (36/107)	24·8%，43·4%		0·94

PBMCs: peripheral blood mononuclear cells. PPS-I: the per-protocol set for immunogenicity; 18 participants of phase 2 (2% and 3% of the vaccine and placebo group, respectively) with baseline cross-reactivity were excluded from the PPS-I. N: the number of participants in PPS-I. n: the number of responders. CI: confidence interval.
*Responders: negative at baseline, positive after vaccination.
† χ^2 test or Fisher's exact test was used to compare the response rates of cellular immunity after vaccination between the groups.

Table S9. The level of spot-forming cells per million PBMCs for IFN-γ in PBMCs of responders* in phase 2 (PPS-I).

Time after the second dose	Participants	Vaccine		Placebo		*P* value†
		n	Median (IQR)	n	Median (IQR)	
28 days						
	Total	211	37·4 (18·0, 64·6)	117	27·4 (16·6, 72·8)	0·31
	18-59 y	134	40·9 (20·0, 70·0)	77	26·6 (15·4, 84·0)	0·076
	≥ 60 y	77	30·6 (16·6, 57·4)	40	31·0 (18·3, 72·4)	0·45
	Pre-existing H1N1-IgG antibody titres < 1:6400	99	39·4 (18·0, 60·6)	63	26·0 (16·6, 72·0)	0·31
	Pre-existing H1N1-IgG antibody titres ≥ 1:6400	112	34·3 (18·3, 69·3)	54	29·7 (15·4, 91·2)	0·70
6 months						
	Total	146	19·4 (13·4, 34·6)	72	24·3 (14·6, 33·6)	0·17
	18-59 y	101	18·8 (13·4, 35·2)	47	24·6 (14·8, 34·6)	0·20
	≥ 60 y	45	20·0 (12·8, 32·0)	25	21·4 (14·0, 32·6)	0·57
	Pre-existing H1N1-IgG antibody titres < 1:6400	68	19·1 (14·0, 36·3)	36	21·1 (14·7, 31·7)	0·48
	Pre-existing H1N1-IgG antibody titres ≥ 1:6400	78	20·4 (12·8, 34·0)	36	27·7 (14·6, 35·0)	0·19

PBMCs: peripheral blood mononuclear cells. PPS-I: the per-protocol set for immunogenicity. n: the number of responders. IQR: interquartile range.

† Wilcoxon rank sum test was used to compare the level of cellular immunity after vaccination between the groups.

*Responders: negative at baseline and positive after vaccination.

Table S10. The level of spot-forming cells per million PBMCs for IFN-γ in PBMCs of responders* in phase 2 (comparison between schedule groups) (PPS-I).

Time after the second dose	0- and 14-days schedule group			0- and 21-days schedule group			0- and 14-days vs 0- and 21- days
	Vaccine	Placebo	*P* value†	Vaccine	Placebo	*P* value†	*P* value†
14 days							
Responder* %(n/N)	20% (45/229)	17% (19/112)	0.55	28% (65/229)	26% (29/110)	0.7	0·029
95%CI	14·7%，25·4%	10·5%，25·2%		22·6%, 34·7%	18·4%, 35·6%		
28 days							
Responder* %(n/N)	44% (100/229)	53% (59/112)	0.12	49% (111/226)	54% (58/108)	0.43	0·24
95%CI	37·1%, 50·4%	43·0%, 62·2%		42·4%, 55·8%	43·8%, 63·3%		
6 months							
Responder* %(n/N)	31% (68/221)	38% (41/109)	0.21	36% (78/215)	30% (31/103)	0.28	0·22
95%CI	24·8%, 37·3%	28·5%, 47·4%		29·8%, 43·1%	21·5%, 39·9%		

PBMCs: peripheral blood mononuclear cells. PPS-I: the per-protocol set for immunogenicity; 18 participants of phase 2 (2% and 3% of the vaccine and placebo group, respectively) with baseline cross-reactivity were excluded from the PPS-I. N: the number of participants in PPS-I. n: the number of responders. CI: confidence interval.

*Responders: negative at baseline, positive after vaccination.

† χ^2 test was used to compare the response rates of cellular immunity after vaccination between the groups.

Table S11. The proportion of specific T-cell immune responders* in PBMCs in phase 2 extension clinical trial (subgroup PPS-I).

Time after the second dose	Participants	Vaccine			Placebo			*P* value†
		Responder* %(n/N)	95%CI	P value†	Responder* %(n/N)	95%CI	P value†	
28 days								
	Total	40% (48/120)	31·2%, 49·3%	-	1% (1/111)	0·0%, 4·9%	-	<0·0001
	18-59 y	39% (25/64)	27·1%, 52·1%	0·82	0% (0/57)	0·0%, 6·3%	0·49	<0·0001
	≥ 60 y	41% (23/56)	28·1%, 55·0%		2% (1/54)	0·0%, 9·9%		<0·0001

PBMCs: peripheral blood mononuclear cells. PPS-I: the per-protocol set for immunogenicity. N: the number of participants in PPS-I. n: the number of responders. CI: confidence interval. *Responders: negative at baseline and positive after vaccination.

† χ^2 test or Fisher's exact test was used to compare the response rates of cellular immunity after vaccination between the vaccine and placebo groups.

Table S12. The level of spot-forming cells per million PBMCs for IFN-γ in PBMCs of responders* in phase 2 extension clinical trial (subgroup PPS-I).

Time after the second dose	Participants	Vaccine		Placebo		*P* value†
		n	Median (IQR)	n	Median (IQR)	
28 days						
	Total	48	59·3 (43·0, 177·0)	1	104·7 (104·7, 104·7)	0·55
	18-59 y	25	58·7 (44·0, 74·0)	0	NA	NA
	≥ 60 y	23	66·0 (41·3, 198·0)	1	104·7 (104·7, 104·7)	0·77

PBMCs: peripheral blood mononuclear cells. PPS-I: the per-protocol set for immunogenicity. n: the number of responders· IQR: interquartile range.

† Wilcoxon rank sum test was used to compare the level of cellular immunity after vaccination between the vaccine and placebo groups.

*Responders: negative at baseline and positive after vaccination. NA: not applicable.

Table S13. Anti-SARS-CoV-2 IgG and s-IgA antibodies at one month after the second vaccination in phase 1 (PPS-I).

Trial	Group	IgG antibody				s-IgA antibody			
		Positive* %(n/N) 95% CI	*P* value†	GMT 95%CI	*P* value‡	Positive* %(n/N) 95% CI	*P*[1] value†	GMT 95%CI	*P* value‡
Phase 1									
	vaccine	25% (13/51) 14%-40%	0·057	3·2 2·5-4·2	NA	12% (6/51) 4%-24%	0·64	4·0 2·1-7·7	NA
	placebo	0% (0/12) 0%-26%		NA		17% (2/12) 2%-48%		NA	

† analyzed with χ^2 test or Fisher's exact test. ‡ analyzed with t test or t' test. *Cut-off titer is 2.

PPS-I: the per-protocol set for immunogenicity. IgG: immunoglobulin G. s-IgA: secretory immunoglobulin A. GMT: geometric mean titre (for positive responders in PPS-I). CI: confidence interval. NA: not applicable.

Table S14. Anti-SARS-CoV-2 IgG and s-IgA antibodies at one month after the second vaccination (ITT).

Trial	Group	IgG antibody				s-IgA antibody			
		Positive* % (n/N)	*P* value†	GMT (95%CI)	*P* value‡	Positive* % (n/N)	*P* value†	GMT (95%CI)	*P* value‡
Phase 1									
	vaccine	25% (13/51)	0·057	3·2 (2·5, 4·2)	NA	12% (6/51)	0·64	4·0 (2·1, 7·7)	NA
	placebo	0% (0/12)		NA		17% (2/12)		NA	
Phase 2									
	vaccine	10% (48/474)	<0·0001	3·8 (3·4, 4·3)	NA	12% (57/474)	<0·0001	3·8 (3·5, 4·1)	0·51
	placebo	0% (0/232)		NA		2% (5/232)		3·5 (1·4, 8·9)	
Phase 2 extension clinical trial (subgroup)									
	vaccine	22% (32*/145)	<0·0001	4·4 (3·3, 5·7)	NA	12% (18/145)	<0·0001	5·2 (4·0, 6·8)	NA
	placebo	1% (1*/148)		NA		0% (0/148)		NA	

† analyzed with χ^2 test or Fisher's exact test. ‡ analyzed with t test or t' test. *Cut-off titer is 2.

ITT: the intention-to-treat set. IgG: immunoglobulin G. s-IgA: secretory immunoglobulin A. GMT: geometric mean titre (for positive responders). CI: confidence interval. NA: not applicable.

Table S15. Anti-SARS-CoV-2 IgG and s-IgA antibodies at one month after the second vaccination (comparison between age groups) (PPS-I).

Trial	Group	IgG antibody			s-IgA antibody		
		Positive* % (n/N)		*P* value†	Positive* % (n/N)		*P* value†
		18-59 y	≥ 60 y		18-59 y	≥ 60 y	
Phase 1							
	vaccine	31% (8/26)	20% (5/25)	0·38	19% (5/26)	4·0% (1/25)	0·19
	placebo	0/6	0/6	NA	33% (2/6)	0/6	0·45
Phase 2							
	vaccine	9% (27/304)	13% (21/162)	0·17	11% (34/304)	14% (23/162)	0·34
	placebo	0/149	0/78	NA	3% (5/149)	0/78	0·17
Phase 2 extension clinical trial (subgroup)							
	vaccine	24% (18/76)	19% (13/67)	0·54	9% (7/76)	16% (11/67)	0·19
	placebo	0/75	0/72	NA	0/75	0/72	NA

† analyzed with χ^2 test or Fisher's exact test. *Cut-off titer: 2.

PPS-I: the per-protocol set for immunogenicity. IgG: immunoglobulin G. s-IgA: secretory immunoglobulin A. NA: not applicable.

Table S16. Anti-H1N1 IgG and s-IgA antibodies at one month after the second vaccination (ITT).

Trial	Group	IgG antibody								s-IgA antibody							
		Responder* %(n/N)	*P* value†	GMT (95%CI) pre	GMT (95%CI) post	*P* value‡	*P* value§	GMI (95%CI)	*P* value§	Responder* %(n/N)	*P* value†	GMT (95%CI) pre	GMT (95%CI) post	*P* value‡	*P* value§	GMI (95%CI)	*P* value§
Phase 1																	
	vaccine	41% (21/51)	>0·99	4681·9 (3833·2, 5718·5)	5511·3 (4430·9, 6855·0)	0·0093	0·74	1·2 (1·0, 1·4)	0·83#	33% (17/51)	0·32	1·1 (1·0, 1·3)	1·6 (1·4, 1·9)	0·0013	<0·0001	1·1 (0·6, 1·9)	0·034
	placebo	42% (5/12)		4031·7 (2513·3, 6467·5)	5079·7 (3436·1, 7509·5)	0·377		1·3 (0·9, 1·7)		17% (2/12)		1·2 (0·9, 1·6)	1·0 (1·0, 1·0)	0·22		0·4 (0·0, 28·9)	
Phase 2																	
	vaccine	33% (156/474)	0·0005	4791·1 (4489·9, 5112·4)	5660·2 (5360·7,5976·4)	<0·0001	0·0027	1·2 (1·1, 1·2)	0·0001	38% (180/474)	<0·0001	1·0 (1·0, 1·0)	1·3 (1·3, 1·4)	<0·0001	<0·0001	1·3 (1·3, 1·4)	<0·0001
	placebo	20% (47/232)		4662·7 (4255·8, 5108·5)	4718·8 (4325·9, 5147·4)	0·738		1·0 (0·9, 1·1)		19% (43/232)		1·0 (1·0, 1·0)	1·1 (1·1, 1·2)	<0·0001		1.1 (1·1, 1·2)	

† analyzed with χ^2 test or Fisher's exact test. ‡ analyzed with paired t test. §: analyzed with t test. # analyzed with Wilcoxon rank sum test. *Responder: a two-fold increase in titer post-vaccination from baseline. Pre-v: pre-vaccination. Post-v: post-vaccination. ITT: the intention-to-treat set. CA4: A/California/4/2009. IgG: immunoglobulin G. s-IgA: secretory immunoglobulin A. GMT: geometric mean titre (for participants in ITT). GMI: geometric mean increase; GMI= GMT_{post} / GMT_{pre}. CI: confidence interval.

Table S17. The positive detection rate of environmental samples.

Sample type	Positive detection rate % (n/N)			
	Room 1	Room 2	Room 3	Room 4
Air				
	46% (26/57)	32% (18/57)	0/57	0/57
Surface				
	27% (20/75)	12% (9/75)	0/75	0/75

The room numbers reported were renumbered by independent sampling investigators.

Table S18. List of protocol deviations.

Trial	Subject ID	GCP Violation	Event	Description	Treatment Measure/Decision
phase 1	1134, 1135, 1136, 1137, 1138	No	The subjects did not attend the visit within the specified time window period	According to the protocol, the window period for the second dose was day 14-15. The 5 subjects received the second dose on day 13, and the sampling time points after the second dose were successively 1 day earlier than the window period specified in the protocol.	Follow-up was continued as required in the protocol. The event did not increase the safety risk of the subjects, did not have a significant impact on any implementation or results of the clinical trial.
	1001, 1002, 1003, 1004, 1005, 1006, 1007, 1008, 1009, 1010, 1011, 1012, 1013, 1014, 1015, 1016, 1017, 1018, 1019, 1020, 1021, 1023, 1025, 1026, 1027, 1028, 1029, 1030, 1031, 1032, 1033, 1034	No	Urine test items were inconsistent with the protocol.	According to the protocol, urine test before and three days after vaccination should include three indicators: "urine protein, urine glucose and urine red blood cell (microscopic examination)". In the first stage (the first dose of 18-59 y), urine test of 32 enrolled subjects only included "urine protein, urine glucose and urinary occult blood". The "urinary occult blood" index was inconsistent with the "urine red blood cell" stipulated in the plan.	None of the 32 subjects showed abnormal occult blood in urine after vaccination. As a qualitative indicator, occult blood can reflect the possibility of red blood cells in urine to a certain extent. The event did not increase the safety risk of the subjects. The event was not considered to have had a significant impact on any implementation or results of the clinical trial.

Trial	Subject ID	GCP Violation	Event	Description	Treatment Measure/Decision
	1110	No	The subject met exclusion criteria for the second dose.	Before the second dose, the subject's blood glucose (fasting) was abnormal (7.25mmol/L, grade 2), which was judged by clinicians to be clinically significant but did not affect vaccination. The subject received the second dose of vaccine and had a blood glucose (fasting) of 7.29mmol/L on October 4, with minimal difference compared with before the second dose of vaccine.	Follow-up was continued as required in the protocol. Additional visits were planned for the subject to continue follow-up of the subject's blood glucose dynamics. The event did not have a significant impact on any implementation or results of the clinical trial.
	1001	No	The subject received other COVID-19 vaccine during the study period	The subject was enrolled on September 1, 2020, and vaccinated in this study on September 1 and September 15, respectively. The investigator was informed on March 14, 2021 that the subject had received another COVID-19 vaccine (Sinovac) on December 20, 2020, and that the subject did not participate in the V4 visit.	The investigator determined that this event might affect the assessment of immunogenicity (at 6 months after the second dose) and concluded that the subject had ended the study early.
phase 2	10125, 10171, 10181, 10215, 10237, 10266, 10301, 10467, 10497, 10542, 10562, 10648,	No	The subjects did not receive the second dose.	The subjects did not receive a second dose because they met the second dose exclusion criteria or refused to receive the second dose.	Follow-up was continued as required in the protocol. The event did not increase the safety risk of the subjects, did not have a significant impact on any

Trial	Subject ID	GCP Violation	Event	Description	Treatment Measure/Decision
	10662, 10702, 10717, 10751				implementation of the clinical trial. But the subjects would be excluded from the per protocol set.
	10356, 10416, 10729, 10782, 10826	No	The subjects received the second dose outside the specified time window period.	The subjects did not receive the second dose within the specified time window period.	Follow-up was continued as required in the protocol. The event did not increase the safety risk of the subjects, did not have a significant impact on any implementation of the clinical trial. But the subjects would be excluded from the per protocol set because the schedule group could not be accurately distinguished.

Trial	Subject ID	GCP Violation	Event	Description	Treatment Measure/Decision
	10301, 10416, 10563, 10564, 10575, 10623, 10633, 10637, 10643, 10667, 10678, 10696, 10725, 10729, 10734, 10746, 10748, 10798, 10820, 10828, 10826, 10741, 10754, 10757, 10769, 10773, 10777, 10820, 10829, 10839, 10840, 10848, 10857, 10866, 10871, 10171, 10181, 10215, 10497, 10562, 10648, 10717, 10083, 10171, 10181, 10215, 10356, 10357, 10497, 10648, 10702, 10717, 10751, 10767, 10083, 10171, 10181, 10205, 10215, 10356, 10357, 10412, 10497, 10536, 10562, 10648, 10702, 10717, 10751, 10767, 10789, 10830,	No	The subjects did not attend the visit within the specified time window period.	The subjects did not complete sample collection or attend the visit within the specified time window period.	Follow-up was continued as required in the protocol. The event did not increase the safety risk of the subjects, did not have a significant impact on any implementation or results of the clinical trial. But if the subject has no any available samples for immunogenicity detection after the second dose, he/she would be excluded from the per protocol set for immunogenicity analysis.

Trial	Subject ID	GCP Violation	Event	Description	Treatment Measure/Decision
	10009, 10045, 10059, 10112, 10132, 10148, 10171, 10181, 10205, 10215, 10356, 10357, 10411, 10412, 10522, 10529, 10562, 10584, 10611, 10620, 10648, 10650, 10702, 10710, 10716, 10717, 10789, 10834, 10835, 10838, 10841				
	10736	No	The subject received other COVID-19 vaccine during the study period	The subject received other COVID-19 vaccine during the interval between V2 (Day 14) and V3 (Day 28).	Follow-up was continued as required in the protocol. The event did not increase the safety risk of the subjects, did not have a significant impact on any implementation of the clinical trial. But the subjects would be excluded from the per protocol set for immunogenicity of V3, V4 and V6.

Trial	Subject ID	GCP Violation	Event	Description	Treatment Measure/Decision
	10092, 10107, 10125, 10127, 10144, 10182, 10193, 10248, 10435, 10565, 10570, 10736, 10836, 10860, 10867	No	The subjects received other COVID-19 vaccine during the study period	The subjects received other COVID-19 vaccine during the interval between V5 (Day 56) and V6 (Day 194).	Follow-up was continued as required in the protocol. The event did not increase the safety risk of the subjects, did not have a significant impact on any implementation of the clinical trial. But the subjects would be excluded from the per protocol set for immunogenicity of V6.
	10322	No	The subject met exclusion criteria.	The subject had been diagnosed with cecal cancer and rectal adenocarcinoma on December 21, 2019 before enrollment. The subject was enrolled on November 20, 2020 without disclosing his cancer history. The investigator was informed on June 7, 2021 that the subject had been hospitalized for chemotherapy on February 26, 2021. After a thorough investigation and history review, the investigator confirmed that the subject met the exclusion criteria NO.13 (Protocol version1.2- 8.3.1).	Long-term safety follow-up was continued as required in the protocol. The event did not increase the safety risk of the subjects, did not have a significant impact on any implementation of the clinical trial. But the subjects would be excluded from the per protocol set.

Trial	Subject ID	GCP Violation	Event	Description	Treatment Measure/Decision
Extension clinical trial	1308	No	Vaccination error	The vaccine number assigned by the random system to the subject was no.3618. However, in the vaccination room, the investigator confused the IP number and wrongly vaccinated the subject with the IP of another subject in the same vaccination room (no. 3611).	Follow-up was continued as required in the protocol. The event did not increase the safety risk of the subjects, did not have a significant impact on any implementation or results of the clinical trial. According to the protocol, the subjects assigned to the same vaccination room would received the same IP (vaccine or placebo), so the subject would not be excluded from the per protocol set.
	1233	No	Randomisation error	The subject was incorrectly stratified due to a randomization error by the investigator.	Follow-up was continued as required in the protocol. The event did not increase the safety risk of the subjects, did not have a significant impact on any implementation of the clinical trial. But the subjects would be excluded from the per protocol set.
	1068, 1131, 1175, 1406, 1409, 1413	No	The subjects did not receive the second dose.	The subjects did not receive a second dose because they met the second dose exclusion criteria or refused to receive the second dose.	Follow-up was continued as required in the protocol. The event did not increase the safety risk of the subjects, did not have a significant impact on any implementation of the clinical trial. But the subjects would be excluded from the per protocol set.

Trial	Subject ID	GCP Violation	Event	Description	Treatment Measure/Decision
	1343	No	The subjects was not vaccinated as per protocol.	The subject received 0.18ml of IP due to insufficient liquid volume of IP, which was less than 0.2ml as stipulated in the protocol.	Follow-up was continued as required in the protocol. The event did not increase the safety risk of the subjects, did not have a significant impact on any implementation or results of the clinical trial.
	1004	No	The subjects was not vaccinated as per protocol.	Because of the operation error of the vaccinator, the IP was fully injected into the subject's right nasal cavity.	Follow-up was continued as required in the protocol. The event did not increase the safety risk of the subjects, did not have a significant impact on any implementation or results of the clinical trial.
	1175, 1307, 1131, 1183, 1330, 1421, 1102, 1170, 1172, 1233, 1288, 1289, 1314, 1348, 1369, 1383, 1387	No	The subjects did not attend the visit within the specified time window period.	The subjects did not complete sample collection or attend the visit within the specified time window period.	Follow-up was continued as required in the protocol. The event did not increase the safety risk of the subjects, did not have a significant impact on any implementation or results of the clinical trial. But if the subject has no any available samples for immunogenicity detection after the second dose, he/she would be excluded from the per protocol set for immunogenicity analysis.

Trial	Subject ID	GCP Violation	Event	Description	Treatment Measure/Decision
	1131, 1030, 1175	No	The subjects received other COVID-19 vaccine during the study period	The subjects received other COVID-19 vaccine during the interval between V1 (Day 0) and V3(Day 56).	Follow-up was continued as required in the protocol. The event did not increase the safety risk of the subjects, did not have a significant impact on any implementation of the clinical trial. But the subjects would be excluded from the per protocol set for immunogenicity.